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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/082,036	02/20/2002	Kathleen A. Elias	09367.0019.01000	9501

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EXAMINER

BRUSCA, JOHN S

ART UNIT	PAPER NUMBER
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1631

DATE MAILED: 10/07/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/082,036	Applicant(s) ELIAS, KATHLEEN A.	
	Examiner John S. Brusca	Art Unit 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 September 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 24-34 and 36-45 is/are pending in the application.
- 4a) Of the above claim(s) 39-42, 44 and 45 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 24-34, 36-38 and 43 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 20 February 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 24-34, and 36-38 are rejected under 35 U.S.C. 102(b) as being anticipated by Hofland et al.

The claims are drawn to a method of predicting the effect of a drug on two different cocultured cells. The effect of the drug is determined by imaging the cells subsequent to exposure to the drug and determining scalar vectors or descriptors from the images. The results are compared to a reference cell. In some embodiments, the effect of the agent is on extracellular matrix deposition, the two cells exhibit a diseased condition, and the two cells are grown in different compartments in the same medium.

Hofland et al. shows in figure 3 a visual assay of cells that were cocultured in a transwell apparatus. The cells were epithelial and fibroblast cells from human breast cancer tissue. The cells were treated with epidermal growth factor. The cells were immunostained to determine the presence of keratin on the extracellular surface. The presence of keratin was used to determine the fraction of cells that are epithelial cells. Hofland et al. shows on page 95 that the analysis of keratin content shows that purification by percoll density gradient fractionation serves to remove most fibroblast cells. Hofland et al. shows that epidermal growth factor and fibroblast cells

enhance growth in breast cancer epithelial cells. Hofland et al. shows in figure 3 staining of control cells with normal rabbit serum in panel b and of cocultured cells throughout.

3. Applicant's arguments filed 01 September 2004 have been fully considered but they are not persuasive. The applicants state that Hofland et al. does not show a quantitative measurement from cell images, however Hofland et al. shows measurement of extracellular keratin levels by immunostaining. The immunostaining assay of Hofland et al. produces a brown color on the cell image when keratin levels are higher than the threshold of detection by the immunostain reagents. The specification states on page 8, lines 5-14 that quantitative cellular phenotypes may comprise measurements of extracellular matrix deposition. On page 3, lines 23-24 the specification states that quantitative representations include scalar values or vectors that characterize morphological or compositional features of a cell. Because Hofland et al. measures the level of extracellular keratin for each cell in the image, a quantitative measure was performed. The claims are not limited to the precision of the quantitative scalar or vector descriptor. In addition, Hofland et al. combines the measurements of each cell in the images to determine an aggregate measurement of keratin-positive cells in pre and post purified cell preparations which is an additional quantitative measurement determined from the image.

4. Claims 24-29, 31-34, and 36-38 are rejected under 35 U.S.C. 102(b) as being anticipated by Stearns et al.

The claims are drawn to a method of predicting the effect of a drug on two different cocultured cells. The effect of the drug is determined by imaging the cells subsequent to exposure to the drug and determining scalar vectors or descriptors from the images. The results are compared to a reference cell. In some embodiments, the effect of the agent is on cell shape.

Stearns et al. shows coculture of human bone marrow endothelial cells and human epithelial prostate cancer cells. The cells are treated with IL-10 in Table 2 and with antibodies to MMP-2 and MMP-9 or antibodies to TIMP-1 in Table 1. Tables 1 and 2 show the results of the cell treatment on image determined length of microvessel formation (as depicted in figure 1). Stearns et al. show in the abstract and throughout that interleukin-10 and MMP-9/MMP-2 antibodies blocked formation of microvessels in the cultured cells. Reference cell comparisons are shown in tables 1 and 2.

5. Applicant's arguments filed 01 September 2004 have been fully considered but they are not persuasive. The applicants state that Stearns et al. do not determine multiple scalar or vector descriptors, however Stearns et al. shows on page 190, column 2 that both the number and length of microvessels were measured, constituting multiple measurements. In addition, Stearns et al. shows on page 190 that multiple measurements were made to allow for a statistically significant observation.

6. Claims 24-34, 36-38, and 43 are rejected under 35 U.S.C. 102(b) as being anticipated by Zietlow et al.

The claims are drawn to a method of predicting the effect of a drug on two different cocultured cells. The effect of the drug is determined by imaging the cells subsequent to exposure to the drug and determining scalar vectors or descriptors from the images. The results are compared to a reference cell. In some embodiments, the effect of the agent is on cell viability, the two cells exhibit a neurodegenerative diseased condition, in some embodiments the cells are neurons and glial cells, in some embodiments the two cells are grown in different compartments in the same medium.

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Zietlow et al. shows in the abstract and figure 1 experiments in which microglial cells and neurons are cocultured in a two-well device that shares a common culture medium. The cells are treated with FMLP. Figure 2 shows the results of imaging the cells for tyrosine hydroxylase antigen by immunofluorescent microscopy as detailed in the methods section in the first column of page 1659. Figure 2 shows the results of viability of tyrosine hydroxylase positive cells after the coculture experiments. Figure 2 shows comparison of the results to control cells.

7. Applicant's arguments filed 01 September 2004 have been fully considered but they are not persuasive. The applicants state that Zietlow et al. only determines a single quantitative value, however Zietlow et al. shows in Figure 2 multiple measurements of independent experiments were combined to generate the quantitative data of each bar graph in figure 2.

Conclusion

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

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9. Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center at (800) 786-9199. Any inquiry concerning this communication or earlier communications from the examiner should be directed to John S. Brusca whose telephone number is 571 272-0714. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael P. Woodward can be reached on 571 272-0722. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JS. Brusca 04 October 2004

John S. Brusca
Primary Examiner
Art Unit 1631

jsb